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<p>(21) International Application Number: <b>PCT/GB97/02588</b></p> <p>(22) International Filing Date: <b>23 September 1997 (23.09.97)</b></p> <p>(30) Priority Data:            96402033.3      25 September 1996 (25.09.96)      EP            (34) Countries for which the regional or international application was filed: <b>FR et al.</b>            97401042.3      9 May 1997 (09.05.97)      EP            (34) Countries for which the regional or international application was filed: <b>FR et al.</b></p> <p>(71) Applicants (for all designated States except US): <b>ZENECA LIMITED [GB/GB]; 15 Stanhope Gate, London W1Y 6LN (GB). ZENECA PHARMA S.A. [FR/FR]; "Le Galien", 1, rue des Chauffours, Boîte postale 127, F-95022 Cergy Cedex (FR).</b></p> <p>(72) Inventors; and            (75) Inventors/Applicants (for US only): <b>THOMAS, Andrew, Peter [GB/GB]; Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). HENNEQUIN, Laurent, François, André [FR/FR]; Zeneca Pharma S.A., Zone Industrielle Sud-Est, Boîte postale 401, F-51064 Reims Cedex (FR). JOHNSTONE, Craig [GB/GB]; Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). STOKES, Elaine, Sophie,</b></p>		<p>Elizabeth [GB/GB]; Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). LOHMANN, Jean-Jacques, Marcel [FR/FR]; Zeneca Pharma S.A., Zone Industrielle Sud-Est, Boîte postale 401, F-51064 Reims Cedex (FR). CLAYTON, Edward [GB/GB]; Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB).</p> <p>(74) Agent: <b>MACK, John, Richard; Zeneca Pharmaceuticals, Intellectual Property Dept., Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB).</b></p> <p>(81) Designated States: <b>AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</b></p> <p><b>Published</b>  <i>With international search report.            Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>

(54) Title: QUINAZOLINE DERIVATIVES AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM

## (57) Abstract

The invention relates to quinazoline derivatives of formula (I) wherein m is an integer from 1 to 2; R<sup>1</sup> represents hydrogen, hydroxy, halogeno, nitro, trifluoromethyl, cyano, C<sub>1</sub>-alkyl, C<sub>1</sub>-alkoxy, C<sub>1</sub>-alkylthio, or -NR<sup>5</sup>R<sup>6</sup> (wherein R<sup>5</sup> and R<sup>6</sup>, which may be the same or different, each represents hydrogen or C<sub>1</sub>-alkyl); R<sup>2</sup> represents hydrogen, hydroxy, halogeno, methoxy, amino or nitro; R<sup>3</sup> represents hydroxy, halogeno, C<sub>1</sub>-alkyl, C<sub>1</sub>-alkoxy, C<sub>1</sub>-alkanoyloxy, trifluoromethyl, cyano, amino or nitro; X<sup>1</sup> represents -O-, -CH<sub>2</sub>-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>7</sup>CO-, -CONR<sup>8</sup>-, -SO<sub>2</sub>NR<sup>9</sup>-, -NR<sup>10</sup>SO<sub>2</sub>- or -NR<sup>11</sup>- (wherein R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup> and R<sup>11</sup> each independently represents hydrogen, C<sub>1</sub>-alkyl or C<sub>1</sub>-alkoxyC<sub>2</sub>-alkyl); R<sup>4</sup> represents an optionally substituted 5 or 6 membered saturated carbocyclic or heterocyclic group or a group which is alkenyl, alkynyl or optionally substituted alkyl, which alkyl group may contain a heteroatom linking group, which alkenyl, alkynyl or alkyl group may carry a terminal optionally substituted group selected from alkyl and a 5 or 6 membered saturated carbocyclic or heterocyclic group, and salts thereof; processes for their preparation, pharmaceutical compositions containing a compound of formula (I) or a pharmaceutically acceptable salt thereof as active ingredient. The compounds of formula (I) and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis.

